

CLAIMS :

1. A method for the crystallization of macromolecules in a three-phase system using a vessel containing a lower aqueous phase, a middle phase and an upper hydrophobic phase having a lower density than that of the lower aqueous phase, wherein an aqueous solution of the macromolecules is added to the middle phase to form a fourth phase, followed by incubation.
2. The method according to claim 1, characterized in that said aqueous solution of macromolecules forms a fourth phase which does not immediately mix with the lower phase.
3. The method according to claim 1 and/or 2, characterized in that said lower phase is a hygroscopic solid phase.
4. The method according to claim 1 and/or 2, characterized in that said lower phase is a hygroscopic liquid phase.
5. The method according to at least one of claims 2 to 4, characterized in that said fourth phase migrates to the phase boundary between the lower and middle phases or to the phase boundary between the middle and upper phases after having been introduced into the vessel.
6. The method according to at least one of claims 2, 3, 4 or 5, characterized in that the vessel is designed in such a way that the fourth phase does not come into contact with the lower phase.
7. The method according to claim 6, characterized in that said fourth phase is located in an indentation and/or compartment.
8. The method according to at least one of claims 2 to 7, characterized in that said fourth phase does not mix completely with the lower phase until the crystallization begins in the fourth phase or at a phase boundary with the fourth phase.

9. The method according to at least one of claims 1 to 8, characterized in that there is essentially no diffusion of water from the vessel through the upper phase over the duration of the crystallization process.
10. The method according to at least one of claims 1 to 9, characterized in that said upper phase contains paraffin oil.
11. The method according to at least one of claims 2 to 10, characterized in that said middle phase is selected to have a diffusion of water from the fourth phase into the lower phase.
12. The method according to at least one of claims 1 to 11, characterized in that said middle phase contains hydroxy-terminated polydimethylsiloxane and/or phenylmethylsilicone oil.
13. The method according to at least one of claims 1 to 12, characterized in that said lower aqueous phase contains salts, buffer substances, polymers and/or organic solvents.
14. The method according to at least one of claims 1 to 13, characterized in that said solution of the macromolecule contains salts, buffer substances, polymers and/or organic solvents.
15. The method according to at least one of claims 1 to 14, characterized in that said macromolecules are proteins, DNA, RNA, complexes of macromolecules, protein complexes, protein/ligand complexes, DNA/ligand complexes, protein/RNA complexes, protein/DNA complexes, viruses or viral fragments.
16. The method according to at least one of claims 1 to 14, characterized in that the crystallization is analyzed and/or continuously monitored by optical measuring methods, especially microphotographs, light scattering methods or spectroscopic methods.

17. Crystals of macromolecules obtained by a method according to any of claims 1 to 16.
18. A device for the crystallization of macromolecules in which a multitude of sample vessels (6, 16) are arranged to form a sample support, wherein said sample support has a contiguous edge (2) which is higher than the openings of the sample vessels, in which at least one subsection (5, 15) separated from the remaining sample vessel by lateral walls (3, 13) exists in each sample vessel (6, 16), wherein the top portions of the lateral walls (3, 13) are lower than the lateral walls of the sample vessel (4, 14).
19. The device according to claim 18, wherein the bottom (1) of the subsections (5) is at the same level as the bottom of the sample vessels (6).
20. The device according to claim 18 and/or 19, wherein the bottom of the sample support is optically homogeneous.
21. A device for the crystallization of macromolecules in which a multitude of sample vessels (6) are arranged to form a sample support, in which at least one subsection (5) separated from the remaining sample vessel by lateral walls (3) exists in each sample vessel (6), wherein the top portions of the lateral walls (3) are lower than the lateral walls of the sample vessel (4), characterized in that the bottom of the sample support is optically homogeneous and that the bottom (1) of the subsections (5) is at the same level as the bottom of the sample vessels (6), wherein said sample support has a contiguous edge (2) which is higher than the openings of the sample vessels.
22. A device for the crystallization of macromolecules in which a multitude of sample vessels (6) are arranged to form a sample support, in which at least two subsections (5) separated from the remaining sample vessel by lateral walls (3) exist in each sample vessel (6), wherein the top portions of the lateral walls (3) are lower than the lateral walls of the sample vessel (4),

wherein the lateral wall or walls of at least one subsection has a different height.

23. The device according to claim 22, characterized in that the bottom of the sample support is optically homogeneous and that the bottom (1) of the subsections (5) is at the same level as the bottom of the sample vessels (6).
24. A three-phase system for the crystallization of macromolecules in which three liquid phases are on top of one another in one vessel, wherein these phases are a lower aqueous phase, a middle phase and an upper hydrophobic phase having a lower density than that of the lower aqueous phase.
25. The three-phase system according to claim 24, wherein said lower phase is a hygroscopic phase of solid and/or liquid nature.
26. Use of a method according to claims 1 to 16, the device according to any of claims 18 to 23 and/or a three-phase system according to claims 24 to 25 for the crystallization of macromolecules, for automated crystallization or for automated screening.
27. Structures of macromolecules established in the analysis of crystals according to claim 17.